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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/581,412	06/01/2006	Christopher John Burns	415852001000	3749

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EXAMINER	
MOORE, SUSANNA	

ART UNIT	PAPER NUMBER
1624	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,412	BURNS ET AL.	
	Examiner	Art Unit	
	SUSANNA MOORE	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,8 and 13-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *18* is/are allowed.

6)☒ Claim(s) *1-5,7,8,13-17 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The instant Application is being examined by a new Examiner

Response to Arguments

Applicant's arguments, see Remarks, filed 10/8/2008, with respect to Office Action mailed 5/14/2008 have been fully considered. If a previous rejection does not appear in the instant Office Action, the rejection has been withdrawn. Thus, this is a Nonfinal Office Action. In summary, claims 1-5, 7, 8 and 13-19 are currently pending and under consideration.

There are 14 claims pending and 14 under consideration. Claims 1-5, 7 and 13-14 are compound claims. Claim 7 is a composition claim. Claim 8 is a method of using claims.

Specification

The disclosure is objected to because of the following informalities: in the middle of pages 12 and 14, C_{1-4} alkyl, aryl and hetaryl are defined as being optionally substituted. The Specification does not provide any definition for the substitutions. Thus, the metes and bounds of the substitution on C_{1-4} alkyl, aryl and hetaryl is unclear. Appropriate correction is required.

Claim Objections

Claim 2 is objected to because of the following informalities: an "or" is needed between "aryl" and "hetaryl" in the definition of A. Appropriate correction is required.

Claim 2 is objected to because of the following informalities: please replace the term "CO_2R8" with "CO_2R^8" at the end of the definition of A. Appropriate correction is required.

Claim 1 is objected to because of the following informalities: please remove the phrase, "and pharmaceutically acceptable salts, hydrates, solvates, crystal forms or diastereomers therof"

at the end of claim 1 since it is repeated in lines 3-4 of claim 1. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 7, 8, 13-17 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1, 2 and 19, the terms "aryl, hetaryl, C_{1-4}aryl, C_{1-4}hetaryl" in the definition of A is vague. There are two definitions for aryl and hetaryl. Furthermore the C_{1-4}aryl and C_{1-4}hetaryl do not exist. Claims which depend from claim 1 which fail to remedy the deficiency of claim 1 are also rejected for the reasons set forth herein.

Regarding claims 1, 7 and 14-16, Q and W are defined twice, See claim 1, page 3, the fourth from the last line at the bottom of the page. Which definition does Applicant intend?

Regarding claims 1, 7 and 14-17, the definition of Q states, "trivalent alkylene." A The variable Q is a linker and thus must be divalent. Is this what Applicant intends?

Claims 1, 7 and 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The definition of Q has changed from a C_{1-4} alkylene to a trivalent alkylene. This is a new matter rejection.

Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 19 does not find support in the disclosure. Applicant remarks, "New claim 19 is a narrower form of claim 1; the definitions of substituents have been imported from claim 1 and the backbone structure clearly conforms to many of the compounds tested as set forth in Table 3." This is not found persuasive. The subgenus and the many combinations found within is not found in the Specification. The species to which Applicant refers are supported but not the new subgenus. This is a new matter rejection.

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The addition of the phrase “and pharmaceutically acceptable salts, hydrates, solvates, crystal forms or diastereomers therof" to claim 3 does not find support in the disclosure. This is a new matter rejection.

Claims 1-5, 7, 8, 13-17 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds of claims 1, 3 or 4 or pharmaceutically acceptable salts of said compound does not reasonably provide enablement for a hydrate, solvate or crystal forms of a compound of claims 1, 3 or 4. The specification does not provide sufficient guidance nor does it enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case:

The nature of the invention

The nature of the invention is a compound of claims 1, 3 or 4, or a pharmaceutically acceptable salt of said compound. There is not a general teaching of solvates of compounds of claims 1, 3 or 4 in the specification.

The state of the prior art and predictability or lack thereof in the art

It is the state of the prior art that the term "solvate" found in the claims is defined as a compound formed by solvation (the combination of solvent molecules with molecules or ions of the solute. It has been estimated that approximately one-third of the pharmaceutically active substances are capable of forming crystalline hydrates. Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates and hence generalizations cannot be made for a series of related compound (See Vippagunta, et al.)

The scope of "solvate" is not adequately enabled or defined. Applicants provide no guidance as how the compounds are made more active in vivo. Solvates can not be predicted and therefore are not capable of being claimed if the applicant cannot properly enable a particular solvate.

The amount of direction or guidance present and the presence or absence of working examples

There is no direction or guidance present in the specification or working examples present in the specification are that defines or relates to what solvates are being included in the elected invention. In pages 24-57, all examples are described as a "solid," "semi-solid" or "oil."

The breadth of the claims

The breadth of the claims is a compound of claims 1, 3 or 4 or pharmaceutically acceptable salts, hydrates, solvates or crystal forms thereof.

The quantity of experimentation needed and the level of the skill in the art

While the level of the skill in the pharmaceutical art is high, the quantity of experimentation needed is undue experimentation. One of skill in the art would need to prepare compounds with various solvents without any direction as to what compounds form solvates with which solvents.

The level of skill in the art is high without showing or guidance as to how to make hydrates, solvates or crystal forms of a conjugate of claims 1, 3 or 4 it would require undue experimentation to figure out the solvents, temperatures and reaction times that would provide hydrates, solvates or crystal forms of the above compounds.

To overcome this rejection, Applicant should submit an amendment deleting the terms "hydrates, solvates, crystal forms" or provide evidentiary support for solvates.

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claim is drawn to the treatment of cancer. The specification does not provide enablement for the treatment of leukemia and lymphoma. No compound has ever been found that can treat leukemia and lymphoma generally even though massive efforts have been directed towards this end. Since this assertion is contrary to what is known in oncology, proof must be provided that this revolutionary assertion has merits. Nearly all anticancer drugs are effective against only a limited group of related cancers. Therefore, a compound effective against leukemia and lymphoma generally would be a revolutionary exception. Applicant is asserting that he succeeded where others have failed. Furthermore, the Specification does not contain any in vivo animal models to treat any disease covered by the scope of leukemia and lymphoma. The instant compounds tested in vitro against JAK2, JAK3, ZAP70, abl, tie2, kdr, btk, fma and hck. Currently there is not an anticancer agent which occurs through the inhibition of any of these proteins. Where extensive efforts have all failed, it is reasonable for the Patent and Trademark Office to require proof that the claimed invention actually works for this specific utility. It is well established that a utility rejection is proper when scope of

enablement is not reasonably correlated to the scope of the claims. (*In re Vaeck* 20 USPQ2d 1439, 1444, *In re Ferens* 163 USPQ 609).

In re Buting 163 USPQ 689 establishes that even clinical tests showing that a compound found to be useful in the treatment of two types of cancers was not sufficient for a much broader range.

The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5, 7, 8, 13-17 and 19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 and 9-13 of copending Application No. 10585916. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds in the '916 application differ only at the R^3 or R^4 substituent, an alkyl verus an alkene. The Specification on pages12 and 14 of the instant Application defined alkyl as a straight or branched C_{1-4} alkyl chain. The saturation is not discussed. Furthermore, the scope of the '916 Application is much broader than the instant Application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSANNA MOORE whose telephone number is (571)272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Susanna Moore/
Examiner, Art Unit 1624